

Amendments to the Claims

The listing of claims will replace all prior versions and listings of claims in the application.

1. (withdrawn) Human polypeptide designated Cyk-4, which is a GTPase activating protein (GAP) for Rho family of GTPases, with the amino acid sequence as set forth in SEQ ID NO:2 or with the amino acid sequence encoded by a polynucleotide which hybridizes under stringent conditions to a polynucleotide having a nucleotide sequence as set forth in SEQ ID NO:1.

2. (withdrawn) Murine Cyk-4 polypeptide designated Cyk-4, which is a GTPase activating protein (GAP) for Rho family of GTPases, with the amino acid sequence as set forth in SEQ ID NO:4 or with the amino acid sequence encoded by a polynucleotide which hybridizes under stringent conditions to a polynucleotide having a nucleotide sequence as set forth in SEQ ID NO:3.

3. (withdrawn) An isolated DNA molecule comprising a polynucleotide with the nucleotide sequence as set forth in SEQ ID NO:1 encoding human Cyk-4 polypeptide, or an isolated DNA molecule encoding human Cyk-4 polypeptide comprising a polynucleotide which hybridizes under stringent conditions to a polynucleotide having a nucleotide sequence as set forth in SEQ ID NO:1.

4. (withdrawn) An isolated DNA molecule comprising a polynucleotide with the nucleotide sequence as set forth in SEQ ID NO:3 encoding murine Cyk-4 polypeptide, or an isolated DNA molecule encoding murine Cyk-4 polypeptide comprising a polynucleotide which hybridizes under stringent conditions to a polynucleotide having a nucleotide sequence as set forth in SEQ ID NO:3.

5. (withdrawn) An antibody which is specifically reactive with an epitope of the human Cyk-4 polypeptide of claim 1.

6. (withdrawn) An antibody which is specifically reactive with an epitope of the murine Cyk-4 polypeptide of claim 2.

7-11. (cancelled)

12. (withdrawn) A compound identified in the method of any one of claims 7 to 11 for use in cancer therapy.

13-44. (cancelled)

45. (new) A method for identifying a compound having the potential to inhibit cytokinesis by determining the compound's ability to inhibit the function of a CYK-4 protein or fragment thereof to promote GTP hydrolysis by a Rho family GTPase, the method comprising:

- (i) incubating the Rho family GTPase with GTP for a period of time sufficient to allow saturation of the Rho family GTPase's GTP binding sites;
 - (ii) adding the CYK-4 protein or fragment thereof to the Rho family GTPase and the GTP in the presence and absence of a test compound, wherein the CYK-4 protein or fragment thereof comprises a GTPase activating protein domain; and
 - (iii) determining an amount of GTP that is hydrolyzed in the presence and absence of the test compound;
- wherein the test compound is identified as a compound having the potential to inhibit cytokinesis if the test compound inhibits the CYK-4 stimulated GTP hydrolysis determined in (iii).

46. (new) The method of claim 45, wherein the Rho family GTPase is a full-length Rho family GTPase protein or a fragment of the Rho family GTPase protein that retains GTPase activity.

47. (new) The method of claim 46, wherein the CYK-4 protein is selected from the group consisting of human CYK-4 (SEQ ID NO:2); a protein with an amino acid sequence encoded by a polynucleotide which hybridizes under stringent conditions to a polynucleotide having a nucleotide sequence as set forth in SEQ ID NO:1; murine CYK-4 (SEQ ID NO:4); and a protein with an amino acid sequence encoded by a polynucleotide which hybridizes under stringent conditions to a polynucleotide having a nucleotide sequence as set forth in SEQ ID NO:3.

48. (new) The method of claim 47, wherein the CYK-4 protein is selected from the group consisting of human CYK-4 (SEQ ID NO:2) and a protein with an amino acid sequence encoded by a polynucleotide which hybridizes under stringent conditions to a polynucleotide having a nucleotide sequence as set forth in SEQ ID NO:1.
49. (new) The method of claim 48, wherein the Rho family GTPase is selected from the group consisting of human RhoA, human RhoB, human RhoC, human RAC1, human RAC2, human RAC3, and human GB25.
50. (new) The method of claim 49, wherein the Rho family GTPase is human RhoA.
51. (new) The method of claim 46, wherein the Rho family GTPase is immobilized on a solid support.
52. (new) The method of claim 46, wherein the GTP is labeled.
53. (new) The method of claim 52, wherein the GTP is labeled with a radioisotope or a fluorescent label.
54. (new). A method for identifying a compound having the potential to inhibit cytokinesis by determining the compound's ability to interfere with the function of CYK-4 protein or a fragment thereof to bind to members of the MKLP1 subfamily of kinesin-like proteins, the method comprising:

(i) incubating a CYK-4 protein or fragment thereof for a period of time with an MKLP1 protein subfamily member, in the presence and absence of a test compound, wherein the CYK-4 protein or fragment thereof comprises a domain that binds MKLP1 subfamily proteins; and

(ii) determining an amount of the MKLP1 protein subfamily member bound to the CYK-4 protein or fragment thereof in the presence and absence of the test compound;

wherein the test compound is identified as a compound having the potential to inhibit cytokinesis if the test compound interferes with the binding of the CYK-4 protein or fragment thereof to the MKLP1 protein subfamily member as determined in (ii).

55. (new) The method of claim 54, wherein the MKLP1 protein subfamily member is a full-length MKLP1 protein or a fragment of the MKLP1 protein subfamily member that comprises a domain that binds the CYK-4 protein.

56. (new) The method of claim 55, wherein the MKLP 1 protein subfamily member is selected from the group consisting of CeM03D4.1b (*C. elegans*; GenBank ID U61955, Protein ID 1397342) and HsMKLP1 (human; GenBank ID X67155; SwissProt Q02241).

57. (new) The method of claim 56, wherein the MKLP 1 protein subfamily member is HsMKLP1.

58. (new) The method of claim 55, wherein the CYK-4 protein is selected from the group consisting of human CYK-4 (SEQ ID NO:2); a protein with an amino acid sequence encoded by a polynucleotide which hybridizes under stringent conditions to a polynucleotide having a nucleotide sequence as set forth in SEQ ID NO:1; murine CYK-4 (SEQ ID NO:4); and a protein with an amino acid sequence encoded by a polynucleotide which hybridizes under stringent conditions to a polynucleotide having a nucleotide sequence as set forth in SEQ ID NO:3.

59. (new) The method of claim 58, wherein the CYK-4 protein is selected from the group consisting of human CYK-4 (SEQ ID NO:2) and a protein with an amino acid sequence encoded by a polynucleotide which hybridizes under stringent conditions to a polynucleotide having a nucleotide sequence as set forth in SEQ ID NO:1.

60. (new) The method of claim 58, wherein the fragment of the CYK-4 protein comprises amino acid residues 1-120.

61. (new) The method of claim 55, wherein the CYK-4 protein or fragment thereof is immobilized on a solid support, and wherein the MKLP1 protein subfamily member or fragment thereof is labeled.

62. (new) The method of claim 61, wherein the label is a radioisotope, a fluorescent label, or a hapten.

63. (new) The method of claim 55, wherein step (i) is performed in solution.

64. (new) A method for identifying a compound having the potential to inhibit cytokinesis by determining the compound's ability to inhibit CYK-4 function by determining the compound's ability to inhibit self association of CYK-4 protein or a fragment thereof, the method comprising:

(i) incubating in the presence and absence of a test compound a first CYK-4 protein or fragment thereof with a second CYK-4 protein or fragment thereof, wherein the first CYK-4 protein or fragment thereof and the second CYK-4 protein or fragment thereof each comprises a domain that mediates CYK-4 protein self-association, and wherein the second CYK-4 protein or fragment thereof is labeled; and

(ii) determining an amount of the second CYK-4 protein or fragment thereof bound to the first CYK-4 protein or fragment thereof;

wherein the test compound is identified as a compound having the potential to inhibit cytokinesis if the test compound inhibits the binding of the first CYK-4 protein or fragment thereof to the second CYK-4 protein or fragment thereof as determined in (ii).

65. (new) The method of claim 64, wherein the first CYK-4 protein is selected from the group consisting of human CYK-4 (SEQ ID NO:2); a protein with an amino acid sequence encoded by a polynucleotide which hybridizes under stringent conditions to a polynucleotide having a nucleotide sequence as set forth in SEQ ID NO:1; murine CYK-4 (SEQ ID NO:4); and a protein with an amino acid sequence encoded by a

polynucleotide which hybridizes under stringent conditions to a polynucleotide having a nucleotide sequence as set forth in SEQ ID NO:3.

66. (new) The method of claim 64, wherein the second CYK-4 protein is selected from the group consisting of human CYK-4 (SEQ ID NO:2); a protein with an amino acid sequence encoded by a polynucleotide which hybridizes under stringent conditions to a polynucleotide having a nucleotide sequence as set forth in SEQ ID NO:1; murine CYK-4 (SEQ ID NO:4); and a protein with an amino acid sequence encoded by a polynucleotide which hybridizes under stringent conditions to a polynucleotide having a nucleotide sequence as set forth in SEQ ID NO:3.

67. (new) The method of claim 66, wherein the first CYK-4 protein is selected from the group consisting of human CYK-4 (SEQ ID NO:2) and a protein with an amino acid sequence encoded by a polynucleotide which hybridizes under stringent conditions to a polynucleotide having a nucleotide sequence as set forth in SEQ ID NO:1.

68. (new) The method of claim 65, wherein the fragment of the first CYK-4 protein comprises amino acid residues 1-120.

69. (new) The method of claim 66, wherein the fragment of the second CYK-4 protein comprises amino acid residues 1-120.

70. (new) The method of claim 64, wherein the first CYK-4 protein or fragment thereof is immobilized on a solid support, and wherein the second CYK-4 protein or fragment thereof is labeled.

71. (new) The method of claim 70, wherein the second CYK-4 protein or fragment thereof is labeled with a radioisotope label, a fluorescent label, a hapten label, a peptide label, or an enzyme label.

72. (new) The method of claim 64, wherein the first CYK-4 protein or fragment thereof is identical to the second CYK-4 protein or fragment thereof.

73. (new) The method of claim 64, wherein the first CYK-4 protein or fragment thereof is different from the second CYK-4 protein or fragment thereof.

74. (new) A method for identifying a compound having the potential to inhibit cytokinesis by determining the compound's ability to inhibit CYK-4 function by determining the compound's ability to inhibit self association of a member of the MKLP1 subfamily of kinesin-like proteins or a fragment thereof, the method comprising:

(i) incubating in the presence and absence of a test compound a first MKLP1 protein subfamily member or fragment thereof with a second MKLP1 protein subfamily member or fragment thereof, wherein the first MKLP1 protein subfamily member or fragment thereof and the second MKLP1 protein subfamily member or fragment thereof each comprises a domain that mediates self-association of MKLP1 subfamily proteins,

and wherein the second MKLP1 protein subfamily member or fragment thereof is labeled; and

(ii) determining an amount of the second MKLP1 protein subfamily member or fragment thereof bound to the first MKLP1 protein subfamily member or fragment thereof;

wherein the test compound is identified as a compound having the potential to inhibit cytokinesis if the test compound inhibits the binding of the first MKLP1 protein subfamily member or fragment thereof to the second MKLP1 protein subfamily member or fragment thereof as determined in (ii).

75. (new) The method of claim 74, wherein the first MKLP1 protein subfamily member or fragment thereof is immobilized on a solid support.

76. (new) The method of claim 74, wherein the second MKLP1 protein subfamily member or fragment thereof is labeled with a radioisotope label, a fluorescent label, a hapten label, a peptide label, or an enzyme label.

77. (new) The method of claim 74, wherein the first MKLP1 protein subfamily member or fragment thereof is identical to the second MKLP1 protein subfamily member or fragment thereof.